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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/498,773 02/05/00 BHAN

A PB-9907

022840 HM12/0607  
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EXAMINER

CRANE, L

ART UNIT

PAPER NUMBER

1623

DATE MAILED:

06/07/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

Office Action Summary	Application No. 09/498,773	Applicant(s) Bham et al.	
	Examiner L. E. Crane	Group Art Unit 1623	

- THE MAILING DATE of this communication appears on the cover sheet beneath  
correspondence address -

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE --3-- MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be filed after six months from the date of this communication.
- If the prior for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 USC §133).

### Status

- ☒ Responsive to communication(s) filed on 04/05/01 (Amdt A).
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

### Disposition of Claims

- ☒ Claims ---1-15--- are pending in the application. Claim(s) --0-- have been cancelled.
- Of the above claim(s) ---0--- is/are withdrawn from consideration.
- ☐ Claim(s) ---0--- is/are allowed.
- ☒ Claims ---1-15--- are rejected.
- ☐ Claim(s) ---0--- is/are objected to.
- ☐ Claim(s) ---0--- are subject to restriction or election requirement.

### Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on --0-- is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on --0-- is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. § 119(a)-(d)

- ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119 (a)-(d).
- ☐ All ☐ Some ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) --0--.
- ☐ received in the national stage application from the International Bureau (PCT Rule 17.2(a)).
- \* Certified copies not received: --0--.

### Attachment(s)

- |  |   |
|--|---|
| <input type="checkbox"/> Information Disclosure Statement(s) PTO-1449, Paper No(s). <u>--0--</u> | <input type="checkbox"/> Interview Summary, PTO-413                     |
| <input type="checkbox"/> Notice of Reference(s) Cited, PTO-892                                   | <input type="checkbox"/> Notice of Informal Patent Application, PTO-152 |
| <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review, PTO-948                 | <input type="checkbox"/> Other: <u>--0--</u>                            |

U.S. Patent Trademark Office

Office Action Summary

PTO-326 (Rev. 04/18/01)  
S. N. 09/498,773

Part of Paper No. 8

Copy for ☒ FILE ☐ APPLICANT

Art Unit 1623

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1600, Art Unit 1623.

- 5        No claims have been cancelled, claims 6 and 8 have been amended, and no new claims have been added as per the amendment filed April 5, 2001.

Claims 1-15 remain in the case.

- 10        Claim 6 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- 15        In claim 6, last line, the term "a 2-cyanoethyl phosphate group" is technically incorrect because it implies that the complete protecting group is "NC-CH<sub>2</sub>-CH<sub>2</sub>-O(PO<sub>2</sub>)O-(PO<sub>2</sub>)-O-;" e.g. that there is a diphosphate linkage. However, if the included term "phosphate" is deleted (-- a 2-cyanoethyl group --), then it would appear that the noted term would say what applicant intends to claim; i.e. -- NC-CH<sub>2</sub>-CH<sub>2</sub>-O-(PO<sub>2</sub>)-O- -- aka a cyanoethyl protected monophosphate group.

- 20        Applicant's arguments with respect to claim 6 have been considered but are moot in view of the new grounds of rejection.

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit 1623

5 "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made."

10 Claims 1-15 are rejected under 35 U.S.C. §103(a) as being unpatentable over Isis Pharmaceuticals '124 (PTO-892 ref. L) in view of Hsiung et al. (PTO-892 ref. R).

15 The instant claims are directed to a method of deprotecting the O-protected phosphotriesters of oligonucleotides by contacting same with a organic amine, particularly diethylamine, with a optional additional step wherein the cyanoethyl-deprotected solid-support-attached oligonucleotide is subjected to ammonia cleavage from said solid support.

20 Isis Pharmaceuticals '124 at p. 2 at line 40, to p. 6 at line 22 discloses the use of many different reagents to cleave cyanoethyl protecting groups from phosphate moieties included with solid-support attached oligonucleotide, and to act as a scavenger of the acrylonitrile generated thereby. Applicant is particularly referred to 7, lines 45-63 wherein the reagent is defined to include the secondary amine piperidine. This reference also discloses at p. 23, Example 21, the two step process wherein cyanoethyl deprotection is 25 followed by ammonolysis to cleave the oligonucleotide from the solid support. However, the ISIS '124 reference does not specifically

## Art Unit 1623

disclose diethylamine as a reagent useful in the cyanoethyl deprotection step.

5 Hsiung et al. particularly at pages 3231 discloses the use of organic amines, including diethylamine in particular, to remove the cyanoethyl protecting group from phosphate triesters oligonucleotide synthesis intermediates in a non-solid-support oligonucleotide synthesis. However, Hsiung et al. does not expressly detail the application of this process to support bound oligonucleotides or include a second process step leading to detachment of the oligonucleotide  
10 from the solid support.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the piperidine-based methodology of ISIS '124 to the selective cyanoethyl deprotection of protected phosphate moieties on support bound oligonucleotides with  
15 an optional subsequent step producing free oligonucleotide by cleavage of the linkage to the solid-support. Similarly it would have been an obvious routine experiment to substitute the secondary amine of the Hsiung et al. reference, diethylamine, in place of piperidine to determine the optimal effect of this substitution on the cyanoethyl  
20 protecting group removal step.

Therefore, the instant claimed process of selective phosphate deprotection would have been obvious to one of ordinary skill in the art having the above cited reference before him at the time the invention was made.

25 Applicant's arguments with respect to claims 1-15 have been considered but are moot in view of the new grounds of rejection.

Art Unit 1623

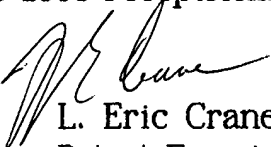
Papers related to this application may be submitted to Group 1600 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone numbers for the FAX machines operated by Group 1600 are (703) 308-4556 and 703-305-3592 .

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is 703-308-4639 . The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Gary Geist, can be reached at (703)-308-1701.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is 703-308-1235 .

LECrane:lec  
06/05/01

  
L. Eric Crane  
Patent Examiner  
Group 1600